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L2	0	(brain or neuron or cord) near4 carboxylesterase	USPAT	OR	OFF	2005/06/15 17:13
L3	0	(brain or neuron or cord) near10 carboxylesterase	USPAT	OR	OFF	2005/06/15 17:13
L4	12	L1 and (brain or neuron or cord)	USPAT	OR	OFF	2005/06/15 17:14

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=> s (brain or neuron or cord) (5A) carboxylesterase
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L4   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2003:829913  CAPLUS
DN   140:176268
TI   Protein and cDNA sequences of 24.64-kilodalton human
     carboxylesterase sequence homolog and their therapeutic uses
IN   Mao, Yumin; Xie, Yi
PA   Bode Gene Development Co., Ltd., Shanghai, Peop. Rep. China
SO   Faming Zhuanli Shenqing Gongkai Shuomingshu, 31 pp.
     CODEN: CNXXEV
DT   Patent
LA   Chinese
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.
DATE
     ---------------      ----   --------    --------------------
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PI   CN 1382799            A     20021204    CN 2001-112736
20010426
PRAI CN 2001-112736                20010426
AB   The invention provides protein and cDNA sequences of a novel
     24.64-kilodalton human protein, designated as "
     carboxylesterase 24.64", which is homologous to carboxylesterase.
     The invention relates to expression of carboxylesterase sequence
homolog
     in E. coli transfected with plasmid encoding the protein.  The
invention
     also relates to preparation of antibody against carboxylesterase
sequence
     homolog.  The invention further relates to the use of the
protein in
     treatment of carboxylesterase sequence homolog-related diseases
(such as
     primary hypertension, peptic ulcer, renopathy syndrome,
bronchial asthma,
     paralysis agitans, etc).

L4   ANSWER 2 OF 12  CAPLUS  COPYRIGHT 2005 ACS on STN
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AN 2001:489645 CAPLUS
DN 135:103447
TI **Human carboxylesterase** 9 and its cDNA and use thereof
IN Mao, Yumin; Xie, Yi
PA Fudan University, Peop. Rep. China; Shanghai Bio Door Gene Technology Ltd.
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001048217	A1	20010705	WO 2000-CN580	20001218
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CN 1300846	A	20010627	CN 1999-125735	19991223
	AU 2001019848	A5	20010709	AU 2001-19848	20001218
PRAI	CN 1999-125735	A	19991223		
	WO 2000-CN580	W	20001218		

AB The invention provides cDNA sequences of a novel **human carboxylesterase** 9 cloned from placenta **brain**. The invention also relates to constructing carboxylesterase 9 gene expression vectors to prepare recombinant carboxylesterase 9 protein using E.coli cells or eukaryotic cells. Methods of expressing and preparing recombinant carboxylesterase 9 protein and its antibody are described. Methods of using carboxylesterase 9 gene or protein products for the treatment of various kinds of diseases, such as cancer, blood diseases, HIV infection,

immune diseases and inflammation are also disclosed.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2000:215924 BIOSIS
DN PREV200000215924
TI cDNA cloning, characterization and stable expression of novel **human brain carboxylesterase.**
AU Hosokawa, Masakiyo [Reprint author]; Mori, Mieko [Reprint author];
Ogasawara, Yuko [Reprint author]; Tsukada, Eiko [Reprint author]; Chiba,
Kan [Reprint author]
CS Lab. Biochem. Pharmacol. Toxicol. Facul. Pharm. Sci, Chiba Univ., Chiba,
263-8522, Japan
SO Japanese Journal of Pharmacology, (2000) Vol. 82, No. Suppl. 1, pp. 114P.
print.
Meeting Info.: 73rd Annual Meeting of the Japanese Pharmacological
Society. Yokohama, Japan. March 23-25, 2000.
CODEN: JJPAAZ. ISSN: 0021-5198.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 31 May 2000
Last Updated on STN: 5 Jan 2002

L4 ANSWER 4 OF 12 MEDLINE on STN DUPLICATE 1
AN 1999448370 MEDLINE
DN PubMed ID: 10518925
TI cDNA cloning, characterization and stable expression of novel **human brain carboxylesterase.**
AU Mori M; Hosokawa M; Ogasawara Y; Tsukada E; Chiba K
CS Laboratory of Biochemical Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Chiba University, Japan.
SO FEBS letters, (1999 Sep 10) 458 (1) 17-22.
Journal code: 0155157. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB025026; GENBANK-AB025028
EM 199910
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991028
AB The DNA sequence encoding a novel **human brain carboxylesterase** (CES) has been determined. The protein is

predicted to have 567 amino acids, including conserved motifs, such as GESAGG, GXXXXEFG, and GDHGD which comprise a catalytic triad, and the endoplasmic reticulum retention motif (HXEL-COOH) observed in CES families. Their gene products exhibited hydrolase activity towards temocapril, p-nitrophenyl-acetate and long-chain acyl-CoA. Since the molecular masses of these gene products are similar to those that exist in capillary endothelial cells of the human brain [Yamamda et al. (1994) Brain Res. 658, 163-167], these CES isozymes may function as a blood-brain barrier to protect the central nervous system from ester or amide compounds.

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:174252 CAPLUS
DN 128:318185
TI Inhibition of **carboxylesterases** in SH-SY5Y **human** and NB41A3 mouse neuroblastoma cells by organophosphorus esters
AU Ehrich, Marion; Correll, Linda
CS Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA, 24061-0442, USA
SO Journal of Toxicology and Environmental Health, Part A (1998), 53(5), 385-399
CODEN: JTEHF8
PB Taylor & Francis
DT Journal
LA English
AB Carboxylesterases (CbxE) can be inhibited by organophosphorus esters (OPs) without causing clin. evidence of toxicity. CbxE are thought to protect the critical enzyme acetylcholinesterase (AChE) from OP inhibition in animals. CbxE and AChE are both present in neuroblastoma cells, but, even though these cells have potential to be an in vitro model of OP toxicity, the effect of OPs on CbxE and the relationship of CbxE inhibition and AChE inhibition have not yet been examined in these cells. Therefore, this study examined concentration-related OP-induced inhibition of CbxE in human SH-SY5Y and mouse NB41A3 neuroblastoma cells with 11 active esterase inhibitors:

paraoxon, malaoxon, chlorpyrifos-oxon, tolyl saligenin phosphate (TSP), Ph
saligenin phosphate (PSP), diisopropyl phosphorofluoridate (DEP), mipafox,
dichlorvos, trichlorfon, dibutyryl dichlorovinyl phosphate (DBVP), and
dioctyl dichlorovinyl phosphate (DOVP). All could inhibit CbxE, although
the enzyme was less likely to be inhibited than AChE following exposure to
9 of the test compds. in the human cell line and to all 11 of the test
compds. in the murine cell line. Species differences in concentration-related
inhibitions of CbxE were evident. When cells were exposed first to an OP
with a low IC50 toward CbxE (PSP), followed by an OP with high affinity
for AChE (paraoxon or malaoxon), inhibitions of CbxE and AChE were
additive. This indicated that CbxE did not protect AChE from OP-induced
inhibition in this cell culture model.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 MEDLINE on STN DUPLICATE 2
AN 95135908 MEDLINE
DN PubMed ID: 7834338
TI Immunohistochemistry with an antibody to **human** liver **carboxylesterase** in **human brain** tissues.
AU Yamada T; Hosokawa M; Satoh T; Moroo I; Takahashi M; Akatsu H; Yamamoto T
CS Department of Neurology, Chiba University, Japan.
SO Brain research, (1994 Sep 26) 658 (1-2) 163-7.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950314
Last Updated on STN: 19980206
Entered Medline: 19950302
AB **Human** liver **carboxylesterase** (CE) is an enzyme capable of metabolizing drugs, and may also function as a regulator of lipid
metabolism. We examined one isoform of CE by immunohistochemistry in the
brains of neurologically normal, Alzheimer disease (AD), amyotrophic
lateral sclerosis (ALS) and cerebral infarction cases. In all but the

infarcted brains, the anti-CE antibody stained only capillary endothelial cells in the brain and spinal cord tissues. In infarct brain areas, intense immunoreactivity of the macrophages was seen. In contrast, the macrophages in the ALS lateral columns and the reactive microglia located in the center of classical senile plaques in AD, as well as other reactive microglial cells in the grey matter, showed no immunoreactivity. In the central nervous system, CE may function as a protective factor against foreign chemicals in capillary endothelial cells, and the antibody to CE may serve as a marker for invading macrophages from the systemic circulation.

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1984:525745 CAPLUS
DN 101:125745
TI The effect of nordihydroguaiaretic acid and related lignans on formyltetrahydrofolate synthetase and carboxylesterase
AU Schegg, Kathleen M.; Welch, William, Jr.
CS Dep. Biochem., Univ. Nevada, Reno, NV, 89557, USA
SO Biochimica et Biophysica Acta (1984), 788(2), 167-80
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB The lignans nordihydroguaiaretic acid (NDGA), heminordihydroguaiaretic acid (HNDGA), and norisoguaiacin inhibited formyltetrahydrofolate synthetase (EC 6.3.4.3) and carboxylesterase (EC 3.1.1.1) activity from a wide variety of sources. In all cases, NDGA was the most effective inhibitor. Synthetase activity was reduced by half at NDGA concns. of 0.11-0.24 mM. Esterase activity consisted of NDGA-sensitive and NDGA-resistant forms. The sensitive class was half-inhibited by 2-4 μM NDGA. Irreversible inhibition of formyltetrahydrofolate synthetase by NDGA was observed both at low protein concentration (<0.2 mg/mL) and at high protein concentration, where precipitation of protein was observed Inhibition of formyltetrahydrofolate synthetase by NDGA arises from a decrease in Vmax and increase in Km for all substrates. In contrast, NDGA affects only the

Vmax parameter of the esterase activity. The broad range of enzymes inhibited by NDGA may be a consequence of the amphipathic character of the mol. and the flexibility to accommodate to a variety of binding sites. The previously reported ability of NDGA to inhibit phagocytosis may be due to the compound's ability to inhibit carboxylesterases.

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1983:501369 CAPLUS
DN 99:101369
TI **Carboxylesterases** in primate **brain**: characterization of multiple forms
AU Chemnitius, J. M.; Zech, R.
CS Med. Fak., Univ. Goettingen, Goettingen, D-3400, Fed. Rep. Ger.
SO International Journal of Biochemistry (1983), 15(8), 1019-25
CODEN: IJBOBV; ISSN: 0020-711X
DT Journal
LA English
AB **Carboxylesterase** activity of primate **brain** (Macaca mulatta) was determined by using Ph valerate (PV) as substrate. Eight **carboxylesterases** of primate **brain** were characterized in respect to PV-hydrolyzing activity and to their inhibition rate consts. for the reaction with organophosphorus compds. Carboxylesterase III was identified as neurotoxic esterase. Organophosphate inhibition data for primate acetylcholinesterase (EC 3.1.1.7) and of primate cholinesterase (EC 3.1.1.8) were determined and compared to corresponding data for primate **brain carboxylesterases**. Physiol. functions and the clin. and toxicol. significance of primate **brain carboxylesterases** are discussed.

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1983:212020 CAPLUS
DN 98:212020
TI Malaoxon sensitivity of esterases from several species of teleosts
AU Gantverg, A. N.; Perevoznikov, M. A.; Rozengart, V. I.
CS Inst. Evol. Physiol. Biochem., Leningrad, USSR
SO Zhurnal Evolyutsionnoi Biokhimii i Fiziologii (1983), 19(2), 191-3
CODEN: ZEBFAJ; ISSN: 0044-4529
DT Journal
LA Russian
AB Malaoxon (I) is an effective inhibitor of esterases from the perch Perca

fluviatilis, pike Esox lucius, carp Cyprinus carpio, and roach Rutilus rutilus. The sensitivity of cholinesterase from the brain of the fishes investigated is practically identical and therefore it cannot account for different resistance of the organism to I poisoning. Different sensitivity of the carp and perch to carbofos is paralleled by different levels of the activity of carboxyesterase in these species. However, significant anticarboxylesterase activity of I may prevent carbofos hydrolysis in fish by carboxylesterase.

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1979:119396 CAPLUS
DN 90:119396
TI **Human** microsomal **carboxylesterase** (E.C. 3.1.1.1.). Distribution in several tissues and some preliminary observations on its appearance in serum
AU Junge, Wolfgang
CS Zentrallab., Staedtisches Krankenhaus Kiel, Kiel, Fed. Rep. Ger.
SO Enzymes Health Dis., Inaug. Sci. Meet. Int. Soc. Clin. Enzymol. (1978), Meeting Date 1977, 54-8. Editor(s): Goldberg, David M.; Wilkinson, John Henry. Publisher: Karger, Basel, Switz.
CODEN: 39YUAE
DT Conference
LA English
AB Carboxyesterase levels were determined in various tissues in nonpathol. and pathol. cases by kinetic and immunol. methods. Carboxysterase was detected in the liver (.apprx.1.2 mg esterase/g tissue) and other organs but not in serum or in any other body fluid in nonpathol. cases. The serum of patients who had elevated levels of enzymes routinely used for diagnosis of liver diseases were examined for carboxylesterase. The enzyme was detected in 30% of the samples at levels of .apprx.20-6800 units/L. The highest activities of carboxylesterase were found in diseases causing acute or subacute liver congestion (acute right heart or global cardiac failure, cardiogenic shock, status asthmaticus, or pulmonary artery

embolism. A profound damage of liver cells with subsequent liberation of the microsomal bound esterase also occurred under various toxic conditions (alc. or drug abuse).

L4 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 3
AN 77157997 MEDLINE
DN PubMed ID: 857894
TI **Carboxylesterases** of **human brain** extract. Purification and properties of a butyrylesterase.
AU Hojring N; Svensmark O
SO Biochimica et biophysica acta, (1977 Apr 12) 481 (2) 500-14. Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197706
ED Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19770630
AB 1. A carboxylesterase (carboxylic-ester hydrolase, EC 3.1.1.1) from human brain extract was prepared to purity using DEAE-cellulose, Sephadex G-200, and fractionation with (NH4)2SO4. The yield was about 20%. 2. Esters of butyric acid were split faster than esters of acetic, propionic and valeric acid, and the enzyme is tentatively designated as a butyrylesterase. Thiocholine esters were split at low rates. 3. The molecular weight was estimated as 340 000 using gel chromatography on Sephadex G-200. In isoelectric focussing the enzyme was resolved into several peaks (pI 4.0--4.7). The low isoelectric point does not seem to be due to terminal sialic acid residues. 4. The enzyme was irreversibly inhibited by diethyl-p-nitrophenyl phosphate (ki = 206 mol-1 - 1 - s-1) and by diisopropylfluorophosphate. The carboxylesterase inhibitor bis-p-nitrophenyl phosphate and eserine did not inhibit the enzyme. 5. The enzyme was progressively inhibited by p-hydroxy-mercuribenzoate, and reactivated by dithiothreitol and 2-mercaptoethanol. N-Ethylmaleimide inactivated the enzyme very slowly, whereas iodoacetate and iodoacetamide

were without effect. 6. Ca2+, Mg2+, and Zn2+ or EDTA did not influence
the enzyme activity.

L4 ANSWER 12 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 4
AN 77145644 EMBASE
DN 1977145644
TI Carboxylesterases with different substrate specificity in human brain
extracts.
AU Hojring N.; Svensmark O.
CS Inst. Biochem. B, Univ. Copenhagen
SO Journal of Neurochemistry, (1976) Vol. 27, No. 2, pp. 523-528.
CODEN: JONRA
DT Journal
FS 029 Clinical Biochemistry
008 Neurology and Neurosurgery
LA English
AB Methods for the determination of carboxylesterase activity in soluble as
well as in particulate samples with p nitrophenylacetate and butyrate and
α naphthylacetate and butyrate as substrates are described. Of the
carboxylesterase activity of **human brain**, 8 to
20% was present in aqueous extracts. Particle bound carboxylesterases
could not be solubilized. By DEAE cellulose chromatography the
carboxylesterases were separated into 6 more or less inhomogeneous
fractions. One of these was further resolved into 2 fractions by
chromatography on CM cellulose. Fractions obtained by ion exchange
chromatography were resolved into several fractions by isoelectric
focusing. Gel chromatography on Sephadex G 200 resolved the
carboxylesterases of **brain** extract into two fractions
(molecular weights about 60,000 and 300,000). At least 4 different types
of carboxylesterases could be distinguished on the basis of different
substrate specificity.

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21: Ulvestad E, Williams K, Matre R, Nyland H, Olivier A, Antel J. Related Articles, Links

Fc receptors for IgG on cultured human microglia mediate cytotoxicity and phagocytosis of antibody-coated targets.
J Neuropathol Exp Neurol. 1994 Jan;53(1):27-36.
PMID: 8301317 [PubMed - indexed for MEDLINE]

22: Chemnitius JM, Dewald K, Kreuzer H, Zech R. Related Articles, Links

Computerized analysis of covalent inhibition kinetics for identification of heart muscle cholinesterase and brain carboxylesterase isoenzymes. Design of differential inhibition assays.
Chem Biol Interact. 1993 Jun;87(1-3):239-44.
PMID: 8343980 [PubMed - indexed for MEDLINE]

23: Araujo DM, Cotman CW. Related Articles, Links

Trophic effects of interleukin-4, -7 and -8 on hippocampal neuronal cultures: potential involvement of glial-derived factors.
Brain Res. 1993 Jan 8;600(1):49-55.
PMID: 8422590 [PubMed - indexed for MEDLINE]

24: Ovnic M, Swank RT, Fletcher C, Zhen L, Novak EK, Baumann H, Heintz N, Ganschow RE. Related Articles, Links

Characterization and functional expression of a cDNA encoding egasyn (esterase-22): the endoplasmic reticulum-targeting protein of beta-glucuronidase.
Genomics. 1991 Dec;11(4):956-67.
PMID: 1783403 [PubMed - indexed for MEDLINE]

☐ **25:** Stohlmacher P. Related Articles, Links

[Aldehyde metabolizing enzymes in the central nervous system and liver--electrophoresis studies of alcoholism]
Beitr Gerichtl Med. 1991;49:143-7. German.
PMID: 1811491 [PubMed - indexed for MEDLINE]

☐ **26:** Hassan NF, Campbell DE, Rifat S, Douglas SD. Related Articles, Links

Isolation and characterization of human fetal brain-derived microglia in in vitro culture.
Neuroscience. 1991;41(1):149-58.
PMID: 1647502 [PubMed - indexed for MEDLINE]

☐ **27:** Houwen RH, Scheffer H, te Meerman GJ, van der Vlies P, Buys CH. Related Articles, Links

Close linkage of the Wilson's disease locus to D13S12 in the chromosomal region 13q21 and not to ESD in 13q14.
Hum Genet. 1990 Oct;85(5):560-2.
PMID: 2227943 [PubMed - indexed for MEDLINE]

☐ **28:** Kugusheva LI, Rozengart VI, Kozenasheva LIa, Kolesova VA. Related Articles, Links

[A comparative study of the effect of vinyl phosphoric acid esters on cholinesterase and carboxylesterase activities in mammals and arthropods]
Zh Evol Biokhim Fiziol. 1990 Jan-Feb;26(1):30-4. Russian.
PMID: 2360379 [PubMed - indexed for MEDLINE]

☐ **29:** Hayes GM, Woodroofe MN, Cuzner ML. Related Articles, Links

Characterisation of microglia isolated from adult human and rat brain.
J Neuroimmunol. 1988 Sep;19(3):177-89.
PMID: 3410964 [PubMed - indexed for MEDLINE]

☐ **30:** Nambu K, Miyazaki H, Nakanishi Y, Oh-e Y, Matsunaga Y, Hashimoto M. Related Articles, Links

Enzymatic hydrolysis of haloperidol decanoate and its inhibition by proteins.
Biochem Pharmacol. 1987 May 15;36(10):1715-22.
PMID: 3593395 [PubMed - indexed for MEDLINE]

☐ **31:** Ojeda VJ, Stokes BA, Lee MA, Thomas GW, Papadimitriou JM, Cala LA, Stevens SM, O'Neill P. Related Articles, Links

Primary cerebral neuroblastomas. A clinicopathological study of

one adolescent and five adult patients.
Pathology. 1986 Jan;18(1):41-9.
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